

AMENDMENTS TO THE CLAIMS

1. (Withdrawn) A Her2 and/or EGFR inhibitor to be administered to a subject determined to show overexpression or activation of Her2 and/or EGFR as a result of a diagnosis of the subject for the expression or activity of Her2 and/or EGFR based on a test for detecting the expression or activity of Her2 and/or EGFR.

2.(Withdrawn) The inhibitor of claim 1 to be administered to a subject determined to show activation of Her2 and/or EGFR as a result of a diagnosis of the subject for the activity of Her2 and/or EGFR based on a test for detecting the activity of Her2 and/or EGFR.

3. (Withdrawn) The inhibitor of claim 1 to be administered to a subject determined to show overexpression or activation of Her2 and EGFR as a result of a diagnosis of the subject for the expression or activity of Her2 and EGFR based on a test for detecting the expression or activity of Her2 and EGFR.

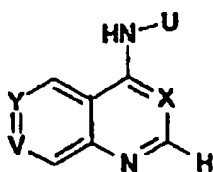
4. (Withdrawn) The inhibitor of claim 3 to be administered to a subject determined to show activation of Her2 and EGFR as a result of a diagnosis of the subject for the activity of Her2 and EGFR based on a test for detecting the activity of Her2 and EGFR.

5. (Withdrawn) The inhibitor of claim 1, wherein the subject is a patient expected to suffer from a disease caused by overexpression or activation of Her2 and/or EGFR.

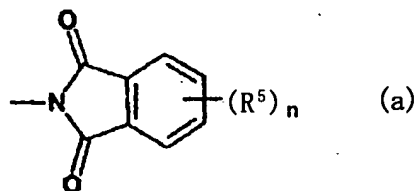
6. (Withdrawn) The inhibitor of claim 1, wherein the subject is a patient expected to suffer from a disease caused by overexpression or activation of Her2 and EGFR.

7. (Withdrawn) The inhibitor of claim 1, wherein the subject is a human.

- 8. (Withdrawn)** The inhibitor of claim 1, wherein the test for detecting the expression or activity of Her2 and/or EGFR is an extracorporeal test.
- 9. (Withdrawn)** The inhibitor of claim 1, wherein the test for detecting the expression or activity of Her2 and EGFR is an extracorporeal test.
- 10. (Withdrawn)** The inhibitor of claim 3, which is a mixture of a Her2 inhibitor and an EGFR inhibitor.
- 11. (Withdrawn)** The inhibitor of any one of claims 1 to 9, which is used for administering a Her2 inhibitor and/or an EGFR inhibitor simultaneously, separately or at time intervals.
- 12. (Withdrawn)** The inhibitor of claim 8 or 9, wherein the extracorporeal test is an immunological method using an antibody, or a hybridization method using a nucleic acid and a nucleic acid derivative.
- 13. (Withdrawn)** The inhibitor of claim 12, wherein the immunological method using an antibody is selected from the group consisting of an enzyme-linked immunosorbent assay, an enzyme-linked immunoassay, a radioimmunoassay, an immunohistochemical method and western blotting.
- 14. (Withdrawn)** The inhibitor of claim 12, wherein the hybridization method using a nucleic acid and a nucleic acid derivative is selected from the group consisting of an RT-PCR method, an ISH method, a FISH method, northern blotting and southern blotting method.
- 15. (Withdrawn)** The inhibitor of any one of claims 1 to 14, which is a substituted heteroaromatic compound represented by the following formula (I)



(I)



(a)

wherein X is N or CH; Y is CR¹ and V is N; or Y is N and V is CR¹; or Y is CR¹ and V is CR²; or Y is CR² and V is CR¹; R¹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, CH₃SO₂CH₂CH₂NHCH₂-Ar- (wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which is optionally substituted by 1 or 2 halogens, C₁₋₄ alkyl or C₁₋₄ alkoxy on demand) or -C≡C-C(R⁶)(R⁷)(R⁸) (wherein R⁶, R⁷ and R⁸ are each independently a hydrogen atom, hydroxy, halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy, or C₃₋₆ cycloalkyl wherein the ring is optionally substituted by hydrogen atom or C₁₋₄ alkyl and optionally contains 1 or 2 hetero atoms selected from O, S and N therein; R² is selected from the group consisting of hydrogen, halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino and -NHCO-R⁹ (wherein R⁹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₄ alkenyl or C₂₋₄ alkynyl); U is phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, each of which is substituted by R³ group and optionally substituted on demand by at least one R⁴ group selected independently; R³ is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and tribenzyloxy and benzenesulfonyl; or R³ is trihalomethylbenzyl or trihalomethylbenzyloxy; or R³ is a group of the above-mentioned formula (a) (wherein each R⁵ is independently selected from halogen, C₁₋₄ alkyl and C₁₋₄ alkoxy; and n is 0-3); each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxy carbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro or trifluoromethyl, or a pharmaceutically acceptable salt thereof, a hydrate or solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof.

16. (Withdrawn) The inhibitor of claim 15, which is (4-(3-fluorobenzyloxy)-phenyl)-(6-(5-((2-methanesulfonyl-ethylamino)methyl)-furan-2-yl)-pyrido[3,4-d]pyrimidin-4-yl)-amine;
(4-benzyloxyphenyl)-(6-(5-((2-methanesulfonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;
N-{4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine;
N-[4-(benzyloxy)phenyl]-7-methoxy-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine;
N-(1-benzyl-1H-indazol-5-yl)-7-methoxy-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine;
N-{3-fluoro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine;
N-[1-(3-fluorobenzyl)-1H-indazol-5-yl]-6-[2-({[2-(methylsulfonyl)ethyl]amino}methyl)-1,3-thiazol-4-yl]-4-quinazolinamine;
6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-N-[4-(phenylsulfonyl)phenyl]-4-quinazolinamine;
N-{3-fluoro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[2-({[2-(methylsulfonyl)ethyl]amino}methyl)-1,3-thiazol-4-yl]-4-quinazolinamine;
N-(1-benzyl-1H-indazol-5-yl)-6-[2-({[2-(methylsulfonyl)ethyl]amino}methyl)-1,3-thiazol-4-yl]-4-quinazolinamine;
N-(3-fluoro-4-benzyloxyphenyl)-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-4-furyl]-4-quinazolinamine;
N-(3-chloro-4-benzyloxyphenyl)-6-[2-({[2-(methylsulfonyl)ethyl]amino}methyl)-4-furyl]-4-quinazolinamine;
N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine;
N-(1-benzyl-1H-indazol-5-yl)-7-fluoro-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-

4-quinazolinamine;

N-(3-trifluoromethyl-4-benzyloxyphenyl)-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-4-furyl]-4-quinazolinamine;

N-[4-(3-chloro-4-fluorophenyl)amino-7-[3-(4-morpholinyl)propoxy]quinazolin-6-yl]acrylamide;

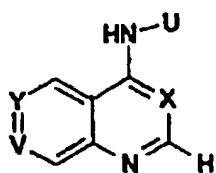
N-{4-[(3-chloro-4-fluorophenyl)amino]-7-[3-methyl-3-(4-methyl-1-piperazinyl)-1-butynyl]-6-quinazolinyl}acrylamide; or

N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methanesulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine, or a pharmaceutically acceptable salt thereof, a hydrate or a solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof.

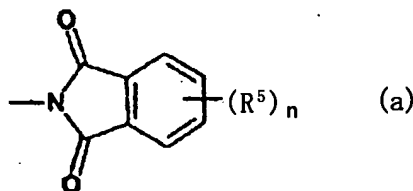
17. (Withdrawn) The inhibitor of claim 15, which is N-[4-(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]quinazolin-6-yl]acrylamide, or N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methanesulfonyl)ethyl]amino}methyl)-2-furyl]-4-quinazolinamine or a pharmaceutically acceptable salt thereof, a hydrate or a solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof.

18. (Withdrawn) A pharmaceutical composition comprising an inhibitor of any one of claims 1 to 17 as an active ingredient and a pharmaceutically acceptable carrier.

19. (Currently Amended) ~~The A~~ pharmaceutical composition of ~~claim 18~~, which is an agent for the prophylaxis and/or treatment of a disease pancreatic cancer, cervical cancer, colorectal cancer, breast cancer, lung cancer, prostate cancer, esophageal cancer, or ovarian cancer caused by overexpression or activation of Her2 and/or EGFR comprising an inhibitor which is a substituted heteroaromatic compound represented by the following formula (I)



(I)



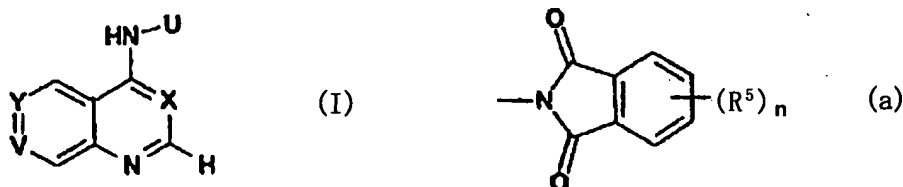
(a)

wherein X is N or CH; Y is CR¹ and V is N; or Y is N and V is CR¹; or Y is CR¹ and V is CR²; or Y is CR² and V is CR¹; R¹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, CH₃SO₂CH₂CH₂NHCH₂-Ar- (wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which is optionally substituted by 1 or 2 halogens, C₁₋₄ alkyl or C₁₋₄ alkoxy on demand) or -C≡C-C(R⁶)(R⁷)(R⁸) (wherein R⁶, R⁷ and R⁸ are each independently a hydrogen atom, hydroxy, halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy, or C₃₋₆ cycloalkyl wherein the ring is optionally substituted by hydrogen atom or C₁₋₄ alkyl and optionally contains 1 or 2 hetero atoms selected from O, S and N therein; R² is selected from the group consisting of hydrogen, halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino and -NHCO-R⁹ (wherein R⁹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₄ alkenyl or C₂₋₄ alkynyl); U is phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, each of which is substituted by R³ group and optionally substituted on demand by at least one R⁴ group selected independently; R³ is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and tribenzyloxy and benzenesulfonyl; or R³ is trihalomethylbenzyl or trihalomethylbenzyloxy; or R³ is a group of the above-mentioned formula (a) (wherein each R⁵ is independently selected from halogen, C₁₋₄ alkyl and C₁₋₄ alkoxy; and n is 0-3); each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxy carbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro or trifluoromethyl, or a pharmaceutically acceptable salt thereof, a hydrate or solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof, and a pharmaceutically

acceptable carrier.

20. (Cancelled)

21. (Currently Amended) An agent for the ~~prophylaxis and/or~~ treatment of pancreatic cancer, cervical cancer, colorectal cancer, breast cancer, lung cancer, prostate cancer, esophageal cancer, or ovarian cancer ~~a disease~~ caused by overexpression or activation of Her2 and/or EGFR, which is to be administered to a subject determined to show overexpression or activation of Her2 and/or EGFR as a result of a diagnosis of the subject for the expression or activity of Her2 and/or EGFR based on a test for detecting the expression or activity of Her2 and/or EGFR, wherein the agent is an inhibitor which is a substituted heteroaromatic compound represented by the following formula (I)

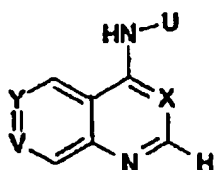


wherein X is N or CH; Y is CR¹ and V is N; or Y is N and V is CR¹; or Y is CR¹ and V is CR²; or Y is CR² and V is CR¹; R¹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, CH₃SO₂CH₂CH₂NHCH₂-Ar- (wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which is optionally substituted by 1 or 2 halogens, C₁₋₄ alkyl or C₁₋₄ alkoxy on demand) or -C≡C-C(R⁶)(R⁷)(R⁸) (wherein R⁶, R⁷ and R⁸ are each independently a hydrogen atom, hydroxy, halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy, or C₃₋₆ cycloalkyl wherein the ring is optionally substituted by hydrogen atom or C₁₋₄ alkyl and optionally contains 1 or 2 hetero atoms selected from O, S and N therein; R² is selected from the group consisting of hydrogen, halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino and -NHCO-R⁹ (wherein R⁹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₄ alkenyl or C₂₋₄ alkynyl); U is phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-

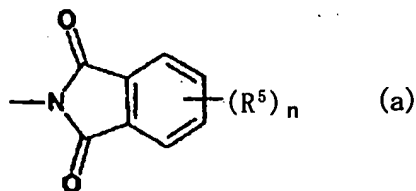
indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, each of which is substituted by R³ group and optionally substituted on demand by at least one R⁴ group selected independently; R³ is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and tribenzyloxy and benzenesulfonyl; or R³ is trihalomethylbenzyl or trihalomethylbenzyloxy; or R³ is a group of the above-mentioned formula (a) (wherein each R⁵ is independently selected from halogen, C₁₋₄ alkyl and C₁₋₄ alkoxy; and n is 0-3); each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxy carbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro or trifluoromethyl, or a pharmaceutically acceptable salt thereof, a hydrate or solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof.

22. (Cancelled)

23. (Currently Amended) A method for the ~~prophylaxis and/or treatment of~~ pancreatic cancer, cervical cancer, colorectal cancer, breast cancer, lung cancer, prostate cancer, esophageal cancer, or ovarian cancer ~~a disease~~ caused by overexpression or activation of Her2 and/or EGFR, which comprises administering an effective dose of a Her2 and/or an EGFR inhibitor to a subject determined to show overexpression or activation of Her2 and/or EGFR as a result of a diagnosis of the subject for the expression or activity of Her2 and/or EGFR based on a test for detecting the expression or activity of Her2 and/or EGFR wherein the inhibitor is a substituted heteroaromatic compound represented by the following formula (I)



(I)



(a)

wherein X is N or CH; Y is CR¹ and V is N; or Y is N and V is CR¹; or Y is CR¹ and V is CR²; or Y is CR² and V is CR¹; R¹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, CH₃SO₂CH₂CH₂NHCH₂-Ar- (wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which is optionally substituted by 1 or 2 halogens, C₁₋₄ alkyl or C₁₋₄ alkoxy on demand) or -C≡C-C(R⁶)(R⁷)(R⁸) (wherein R⁶, R⁷ and R⁸ are each independently a hydrogen atom, hydroxy, halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy, or C₃₋₆ cycloalkyl wherein the ring is optionally substituted by hydrogen atom or C₁₋₄ alkyl and optionally contains 1 or 2 hetero atoms selected from O, S and N therein; R² is selected from the group consisting of hydrogen, halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino and -NHCO-R⁹ (wherein R⁹ is C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₄ alkenyl or C₂₋₄ alkynyl); U is phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, each of which is substituted by R³ group and optionally substituted on demand by at least one R⁴ group selected independently; R³ is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and tribenzyloxy and benzenesulfonyl; or R³ is trihalomethylbenzyl or trihalomethylbenzyloxy; or R³ is a group of the above-mentioned formula (a) (wherein each R⁵ is independently selected from halogen, C₁₋₄ alkyl and C₁₋₄ alkoxy; and n is 0-3); each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxy carbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro or trifluoromethyl, or a pharmaceutically acceptable salt thereof, a hydrate or solvate thereof, an optically active substance or a racemate thereof, or a mixture of diastereomers thereof.

24. (Cancelled)

25. (Withdrawn) A commercial package comprising the pharmaceutical composition of any one of claims 18 to 20 and a written matter associated therewith, the written matter stating that the pharmaceutical composition can or should be used for the prophylaxis and/or treatment of a disease caused by overexpression or activation of Her2 and/or EGFR.

26. (Withdrawn) The commercial package of claim 25, wherein the disease caused by overexpression or activation of Her2 and/or EGFR is cancer, angiogenesis associated with the growth of cancer or sarcoma, angiogenesis associated with cancer metastasis, angiogenesis associated with diabetic retinopathy, arteriosclerosis or psoriasis.